



Use of Abnobaviscum to treat refractory seroma after breast reconstruction with a latissimus dorsi flap: A case report

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In recent years, there has been a notable increase in the rate of refractory donor site seroma, defined as seroma that persists for at least 3 months postoperatively, as the number of breast reconstructions using a latissimus dorsi (LD) musculocutaneous flap has increased. Various factors have been proposed to be related, including smoking, obesity, flap mass, and body weight, and several studies have been conducted to explore treatment methods. Typically, surgical treatment, such as capsulectomy, has been considered for refractory seroma, but in this case report, we describe positive outcomes achieved by using Abnobaviscum to treat three female patients who developed a donor site seroma at least 3 months after breast reconstruction using an LD flap.

Keywords Abnobaviscum / Latissimus dorsi musculocutaneous flap / Mammoplasty / Seroma

INTRODUCTION

With advances in diagnostic techniques for breast cancer, the number of mastectomies has increased over the last few decades, and alongside growing cosmetic interest, this has led to an increase in the frequency of breast reconstruction surgery. The latissimus dorsi (LD) musculocutaneous flap is often used in breast reconstruction, because it enables a natural-looking reconstruction that maintains symmetry with the contralateral side. Although LD flap breast reconstruction has become more common, refractory donor site seroma has been established to be a difficult postoperative complication. Currently, various methods are used to treat seroma, includ-

ing needle aspiration, compression therapy using bandages, arm fixation, triamcinolone injection, and capsulectomy [1-5].

Surgical treatment of refractory seroma using capsulectomy is invasive and provokes anxiety in patients. Therefore, interest has emerged in methods of whole-capsule sclerotherapy for use before considering surgical methods. In the field of thoracic surgery, Abnobaviscum is used to treat adhesions in cases of malignant pleural effusion, and an attempt has been made to use this product to treat seroma [6]. Some studies have reported Abnobaviscum to be effective against malignant pleural effusion, and its efficacy as a sclerosing agent has also been recognized [7-9]. Similarly, there have been continual efforts to treat refractory seroma after malignant pleural effusion treatment or LD flap breast reconstruction using fibrin glue, triamcinolone, anti-inflammatory drugs, or phenytoin [10-14]. At Kyungpook National University Hospital, we have observed positive outcomes when using Abnobaviscum, which has been demonstrated to be safe when used as an anticancer agent, to treat refractory seroma that did not respond to compression dressing using elastic bands, triamcinolone injection, or needle aspiration. Herein, we introduce Abnobaviscum as a potential method to resolve seroma, which is a common complication of LD flap breast reconstruction.

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CASE REPORTS

This was a retrospective, single-center study including three Korean patients who underwent LD flap breast reconstruction and had a refractory seroma between September 2016 and May 2018. The study protocol was approved by the Institutional Review Board on December 31, 2018 (IRB No. 2018-12-017) at Kyungpook National University Chilgok Hospital.

The procedure in this study was performed by a single plastic and reconstructive surgeon. The patient group was limited to patients with refractory seroma that persisted for at least 3 months after LD flap breast reconstruction, and that did not respond to conventional methods, such as compression dressing using elastic bands, needle aspiration, or triamcinolone injection (Table 1). In this patient group, consent was obtained from three patients, who decided to receive treatment with Abnobaviscum (Abnoba Heilmittel GmbH, Pforzheim, Germany) after a thorough explanation. The protocol for using Abnobaviscum is shown in Table 2. A safe dose with regard to adverse effects was determined based on the patient's body weight and the site of administration [5,6], and treatment proceeded according to the method presented below. In patients who showed no response to triamcinolone therapy, 1 mg/ 0.5 mL of Abnobaviscum was mixed with 10 mL of normal saline and administered to the patient. Thereafter, the patient lay in the supine, decubitus right, and decubitus left positions for 10 minutes each, and the Abnobaviscum was removed by aspiration 30 minutes later. Outpatient follow-up was performed 3 days after the procedure; if seroma was observed, the patient visited twice a week for outpatient aspiration, following by compression therapy using elastic bands. After 2 weeks, if the seroma still had not resolved, an identical dose of Abnobaviscum was administered, and for refractory seroma, the Abnobaviscum was administered at a higher dose.

Case 1

A 56-year-old female patient was diagnosed with invasive ductal carcinoma (IDC) of the right breast. The department of surgery decided to perform total mastectomy, and referred her to the de-

Table 1. Patient information

Variable	Result
Age (yr)	52
BMI (kg/m ²)	24.73
Flap size (width×length, cm ²)	5.7×16
Flap weight (g)	240
Breast volume (mL)	
Right breast	260
Left breast	260

Values are presented as mean.

partment of plastic and reconstructive surgery for breast reconstruction. Following an outpatient consultation at the department of plastic and reconstructive surgery, the patient underwent volumetry, and LD flap breast reconstruction was selected as a suitable method for moderate-sized breasts. Following total mastectomy, the patient underwent LD flap breast reconstruction at the department of plastic and reconstructive surgery. On the 13th postoperative day, the daily output drainage was confirmed to be less than 30 mL, and the back drain was removed. No seroma was observed in outpatient follow-up at 3, 4, 6, 8, and 10 weeks postoperatively. At 12 weeks postoperatively, the patient developed refractory seroma and aspiration was performed (Fig. 1). Triamcinolone injections were injected twice in 1 month and, since the seroma did not resolve, according to our institutional protocol, we decided to treat the patient with Abnobaviscum. At 4 months postoperatively, 1 mg of Abnobaviscum was administered, and a second dose of 4 mg was administered at 18 weeks postoperatively. The seroma had completely resolved at 19 weeks postoperatively, and thereafter the patient showed no refractory seroma for a further year after treatment. The total treatment duration was 19 days.

Case 2

A 50-year-old female patient showed clustered microcalcifications in seven locations in her left breast, and was diagnosed with IDC. The department of surgery decided to perform left nipple-sparing mastectomy with sentinel lymph node biopsy, and referred the patient to the department of plastic and reconstructive surgery for breast reconstruction. After consultation with the patient, we decided to perform LD flap breast reconstruction. On October 18, 2016, the patient underwent nipple-sparing mastectomy followed by LD flap breast reconstruction. There were no notable events during surgery. On the 13th postoperative day, the daily output drainage was confirmed to be less than 30 mL, and the back drain was removed. At follow-up, a seroma was observed at the back-donor site, measuring 8 and 6 mL, respectively, on the 10th and 14th days after discharge. Following needle aspiration and triamcinolone injection, back donor site seroma was not observed during four follow-up examinations at 4, 6, 8, and 12 weeks after treatment. At 18 weeks postoperatively, the patient developed a refractory seroma. During the next 12 weeks postoperatively, the patient

Table 2. Protocol for Abnobaviscum use at KNUH

Abnobaviscum treatment protocol (KNUH)			
1st	Abnobaviscum, 1 mg	NS 10 mL mix	3 Weeks later
2nd	Abnobaviscum, 2 mg	NS 10 mL mix	3 Weeks later
3rd	Abnobaviscum, 4 mg	NS 10 mL mix	Finish

The seroma is extracted with a syringe, the mixed fluid is injected into the empty space, and the mixture is withdrawn after 30 minutes. KNUH, Kyungpook National University Hospital; NS, normal saline.

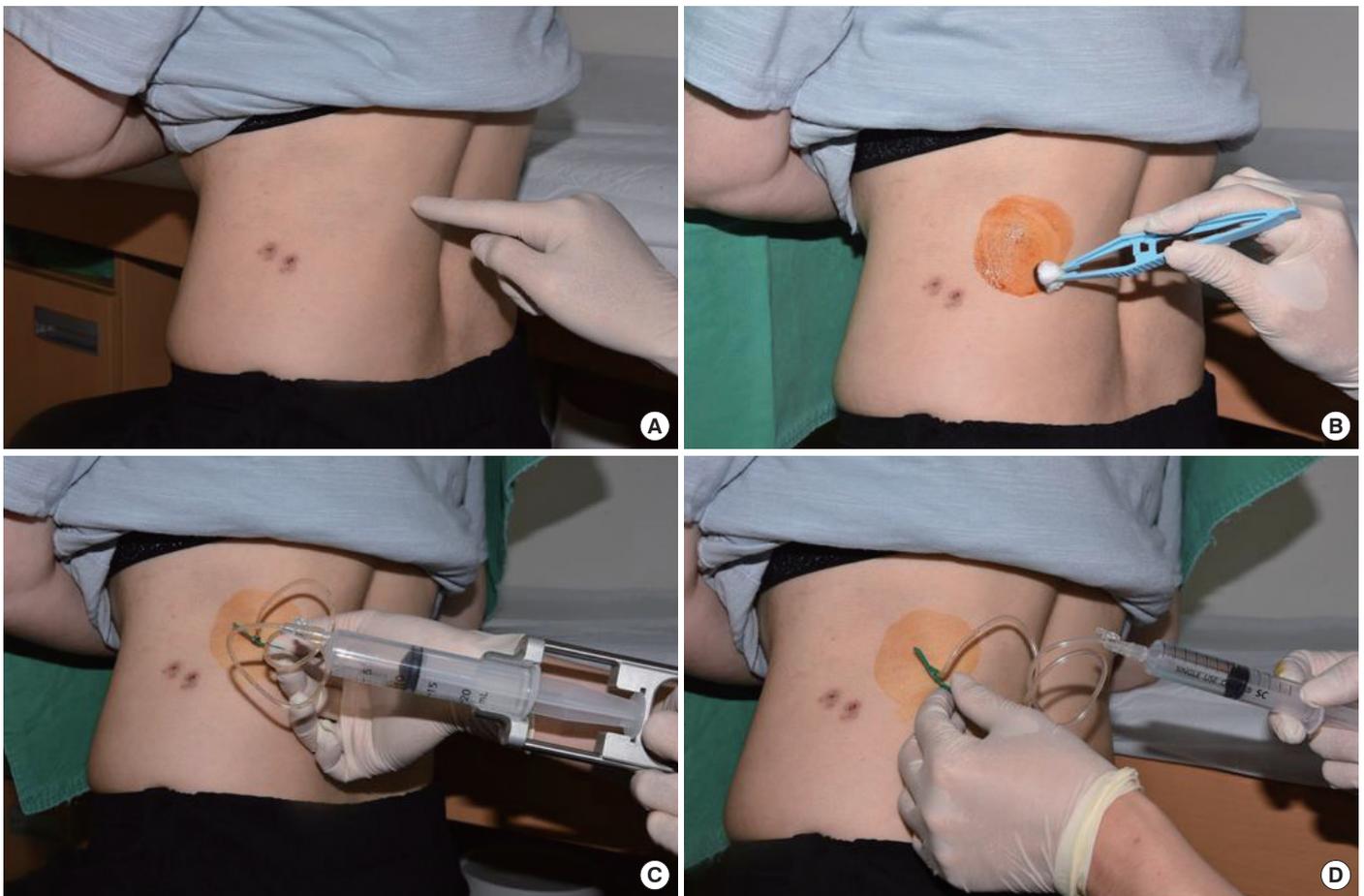


Fig. 1. A 56-year-old woman presented 3 months after breast reconstruction with an extended latissimus dorsi flap. (A) The seroma was checked using ultrasonography and a physical examination. (B) The area was covered with potadine ointment. (C) Aspiration with a needle and syringe. (D) Abnobaviscum injection.

underwent triamcinolone and needle aspiration therapy, as well as compression therapy using elastic band dressings, but an 11-mL seroma continued to be observed up to 30 weeks postoperatively. Triamcinolone therapy was judged to have failed, and so, according to the protocol, we decided to use Abnobaviscum to treat the refractory seroma. The patient received a 1-mg dose of Abnobaviscum at 30 weeks postoperatively, and when the seroma continued to be observed, received another dose of 4 mg at 34 weeks postoperatively. The seroma was cured at 34 weeks postoperatively, after which the patient showed no refractory seroma for a further year after treatment. The total treatment duration was 33 days.

Case 3

A 51-year-old female patient visited the outpatient department complaining of a mass, and was diagnosed with multiple microcalcifications in her left breast; after core needle biopsy, the patient was diagnosed with invasive carcinoma with ductal and lobular features. From October 8, 2016 to January 31, 2017, the patient underwent six rounds of neoadjuvant chemotherapy using docetaxel,

Neoplatin, Herceptin, and Perjeta, and showed complete remission; the patient was then scheduled for surgery. The department of surgery decided to perform total mastectomy, and referred the patient to the department of plastic and reconstructive surgery for breast reconstruction. Following an outpatient visit to the department of plastic and reconstructive surgery, the patient underwent volume-etry, and after consultation with the patient, we decided to perform LD flap breast reconstruction. Surgery was completed with no particular incidents. The patient then underwent radiotherapy and hormonal therapy (Herceptin) from March 13, 2017 to October 2, 2017, under the joint care of the departments of radiation oncology and hematology and medical oncology. At six subsequent follow-up consultations, no seroma was detected at the back-donor site. At 24 weeks postoperatively, the patient developed refractory seroma, which we decided to treat with Abnobaviscum. The patient was administered 2 mg of Abnobaviscum at 25 weeks postoperatively, and since no effect was observed, the dose was increased to 4 mg for subsequent administration at 26, 28, and 31 weeks postoperatively. The seroma had still not resolved; therefore, the dose was increased

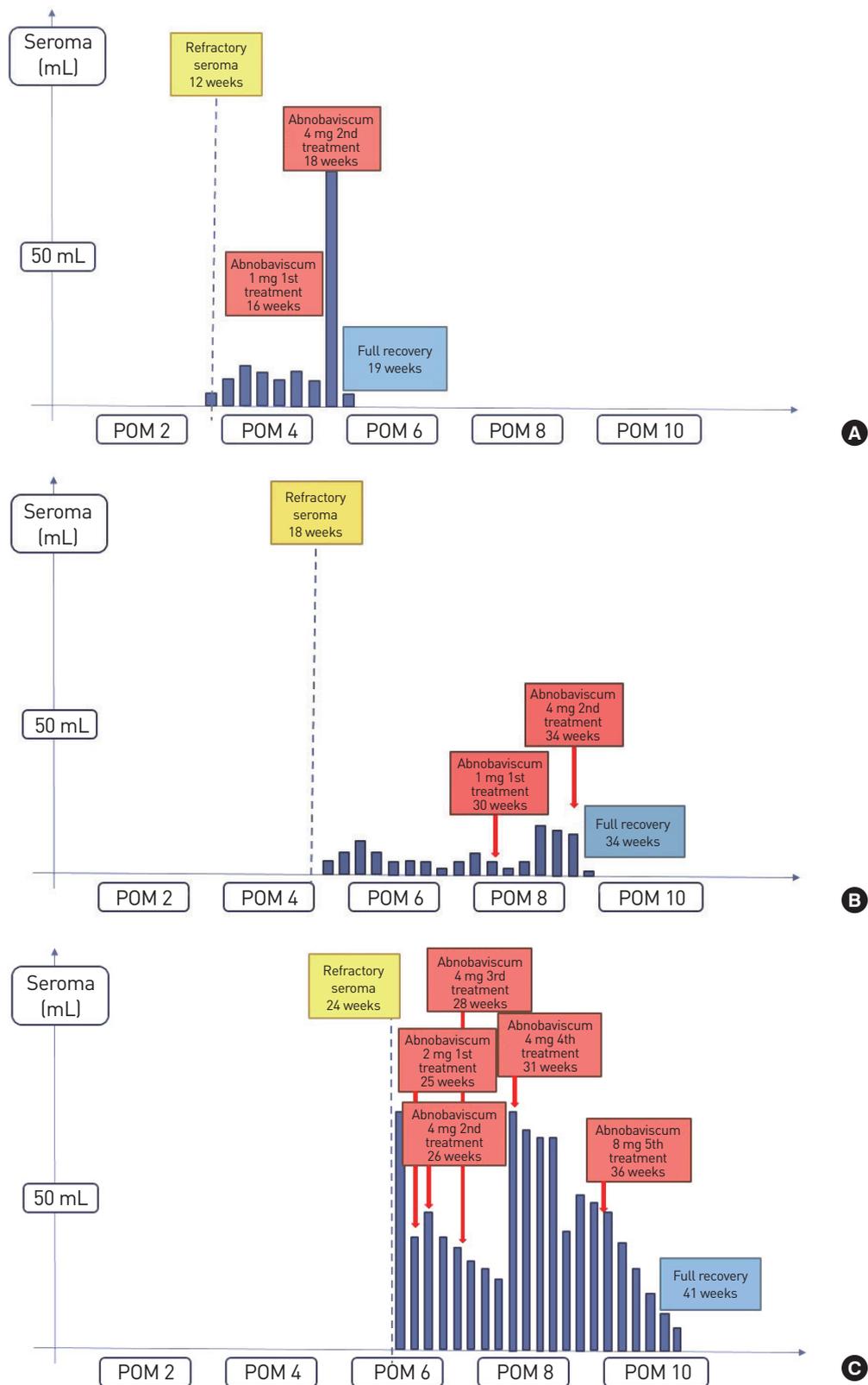


Fig. 2. (A) Graph of seroma severity over time for the case 1, a 56-year-old woman. (B) Graph of seroma severity over time for the case 2, a 50-year-old woman. (C) Graph of seroma severity over time for the case 3, a 51-year-old woman. POM, postoperative month.

again and the patient was administered 8 mg at 36 weeks postoperatively. The seroma had resolved at 41 weeks postoperatively, and no refractory seroma occurred in 28 weeks after treatment. The total duration of treatment was 130 days.

For the three patients in this study, the mean time until use of Abnobaviscum was 5.6 months, the mean duration of treatment was 60.6 days, the mean number of doses was 3, and the patients showed a 100% cure rate with a mean follow-up period of 7 months. The 56-year-old patient developed a mild fever of 38.3°C the day after Abnobaviscum administration, which lasted for about 2 days. This complication has also been mentioned several times in thoracic surgery cases using Abnobaviscum, with mild fevers of less than 39°C that subsided spontaneously (Fig. 2).

DISCUSSION

Abnobaviscum binds to cell membrane receptor proteins, on which it exerts an antitumor effect by dissolving ribosomal RNA, blocking protein synthesis, and inducing cell death. In addition, it promotes macrophage colony-stimulating factor production by lymphocytes; increases levels of interferon, interleukin, tumor necrosis factor, and natural killer cells; enhances immune function; and promotes endorphin secretion [15]. Among the side effects of Abnobaviscum, we focused on the fact that it tends to induce adhesion, and we anticipated that it could be effective when used in patients with a refractory seroma at the donor site after LD flap harvesting for breast reconstruction.

We implemented sclerotherapy, using the method described above, in three patients with refractory donor site seroma that persisted for at least 3 months after LD flap surgery, and that did not respond to conventional methods of compression dressing using elastic bands, needle aspiration, or triamcinolone injection. The three patients showed a 100% full recovery rate with a mean of 60.6 days of treatment and three doses of Abnobaviscum. One patient experienced the adverse effects of a tingling sensation and a mild fever of 38.3°C, but these subsided within 2 days.

For patients in whom conventional treatment failed, adding sclerotherapy using Abnobaviscum before capsulectomy (surgical treatment) could provide a good alternative in patients who experience fear or anxiety related to capsulectomy.

This study has some limitations. First, the injection was processed with a different capacity among patients. Our hospital's treatment method differed from the suggested method. We attempted to optimize the dosage considering patients' body mass index, the amount of seroma, and complications, and we succeeded, with a cure rate of 100% using our method. On this basis, an institutional protocol was established, and patients with the complication of refractory seroma have been treated with this protocol.

Second, limitations of this study include the small number of patients and the short follow-up period. In addition, there was a

lack of observations of clinical outcomes regarding adverse effects when the drug was administered to treat seroma. One 56-year-old female patient showed a mild fever of 38.3°C after Abnobaviscum administration, as well as a tingling sensation. Abnobaviscum has been reported to cause adverse effects of fever, lymph node swelling, and rarely, diarrhea and an increased urge to urinate. Of these, fever is the most common adverse effect, but antipyretic medication should be avoided. If the fever lasts longer than 3 days, differential diagnoses must be considered. Thus, if the reaction exceeds a tolerable level, the subsequent injection should only be given when the fever has regressed, with a reduced concentration and dose. In the context of ongoing research into mechanisms of resolving seroma and pathological changes, as well as treatments and interventions, Abnobaviscum shows the potential to be easy and convenient to use in patients who show no response to conventional therapy or steroid infiltration, but who do not fit the indications for surgical treatment. Abnobaviscum can be a good option to try before surgical treatment, since it reduces patients' anxiety, has only relatively minor complications (such as fever), and is effective at curing refractory seroma.

NOTES

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Ethical approval

The study was approved by the Institutional Review Board of Kyungpook National University Chilgok Hospital (IRB No. 2018-12-017) and performed in accordance with the principles of the Declaration of Helsinki.

Patient Consent

The patients provided written informed consent for the publication and the use of their images.

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REFERENCES

1. Yan WH, Mang JB, Ren LL, et al. Natural history of seroma following

- the immediate latissimus dorsi flap method of breast reconstruction. *Chin Med J (Engl)* 2018;131:1674-9.
2. Hart AM, Duggal C, Pinell-White X, et al. A prospective randomized trial of the efficacy of fibrin glue, triamcinolone acetonide, and quilting sutures in seroma prevention after latissimus dorsi breast reconstruction. *Plast Reconstr Surg* 2017;139:854e-863e.
 3. Lee J, Bae Y, Jung JH, et al. Effects of quilting suture interval on donor site seromas after breast reconstruction with latissimus dorsi muscle flap: a randomized trial. *Clin Breast Cancer* 2016;16:e159-64.
 4. Sowa Y, Numajiri T, Kawarazaki A, et al. Preventive effects on seroma formation with use of the harmonic focus shears after breast reconstruction with the latissimus dorsi flap. *J Plast Surg Hand Surg* 2016; 50:349-53.
 5. Burgic M, Bruant Rodier C, Wilk A, et al. Complications following autologous latissimus flap breast reconstruction. *Bosn J Basic Med Sci* 2010;10:65-7.
 6. Park JB, Lee SA, Lee WS, et al. The management of chemical pleurodesis with *Viscum album* in patients with persistent air leakage. *J Thorac Dis* 2018;10:371-6.
 7. Eom JS, Kim TH, Lee G, et al. Chemical pleurodesis using mistletoe extracts via spray catheter during medical thoracoscopy for management of malignant pleural effusion. *Respirol Case Rep* 2017;5:e00227.
 8. Deliorman D, Calis I, Ergun F, et al. Studies on the vascular effects of the fractions and phenolic compounds isolated from *Viscum album ssp. album*. *J Ethnopharmacol* 2000;72:323-9.
 9. Cho JS, Na KJ, Lee Y, et al. Chemical pleurodesis using mistletoe extraction (ABNOVAviscum[®]) injection for malignant pleural effusion. *Ann Thorac Cardiovasc Surg* 2016;22:20-6.
 10. Harada RN, Pressler VM, McNamara JJ. Fibrin glue reduces seroma formation in the rat after mastectomy. *Surg Gynecol Obstet* 1992;175: 450-4.
 11. Taghizadeh R, Shoaib T, Hart AM, et al. Triamcinolone reduces seroma re-accumulation in the extended latissimus dorsi donor site. *J Plast Reconstr Aesthet Surg* 2008;61:636-42.
 12. Turel KS, Dilek ON, Akbulut G, et al. Effects of local anti-inflammatory drugs on seroma formation after mastectomy and axillary lymph node dissection in the rat model. *Natl J Med Res* 2014;4:228-31.
 13. Eser M, Tural F, Kement M, et al. Effects of local phenytoin on seroma formation after mastectomy and axillary lymph node dissection: an experimental study on mice. *BMC Surg* 2012;12:25.
 14. Ahn HY, Cho JS, Kim YD, et al. Efficacy of mistletoe for chemical pleurodesis in rats without malignancy. *Open Med (Wars)* 2015;10:346-51.
 15. Song KS, Keum D, Kim JB. Chemical pleurodesis using doxycycline and *Viscum album* extract. *Korean J Thorac Cardiovasc Surg* 2017; 50:281-6.